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THROMBOSIS OF THE CORONARY ARTERIES

JAMES B. HERRICK, M.D.

CHICAGO

In a paper¹ on certain clinical features of sudden obstruction of the coronary arteries, read six years ago before the Association of American Physicians, I called attention to the fact that while such obstruction as by a thrombus was very often suddenly fatal, it was not necessarily so; for the coronary arteries were not in the strictest sense terminal arteries; there were often anastomoses capable of reestablishing circulation in the infarcted area to such an extent as to enable the heart to functionate for a time at least. This had been shown by anatomic study of the coronaries, by necropsy observations by the pathologists, by experimental ligation of these vessels, and by clinical experience controlled by post-mortem examinations.

A tentative grouping of the cases of coronary thrombosis based on clinical symptoms was made:

1. Cases of instantaneous death, a group graphically described by Krehl, in which there is no death struggle, the heart beat and breathing stopping at once.
2. Cases of death within a few minutes or a few hours after the obstruction. These are the cases that are found dead or clearly in the death agony by the physician who is hastily summoned.
3. Cases of severity in which, however, death is delayed for several hours, days or months, or recovery occurs.
4. A group that may be assumed to exist embracing cases with mild symptoms, for example, a slight precordial pain

1. Herrick, J. B.: Clinical Features of Sudden Obstruction of the Coronary Arteries, *J. A. M. A.* 59: 2015 (Dec. 7) 1912.

ordinarily not recognized, due to obstruction in the smallest branches of the arteries.

It was Group 3 whose clinical phenomena were discussed, as illustrative of which a few cases were briefly cited, including one with necropsy findings.

These cases of coronary thrombosis are, as it seems to me, of commoner occurrence than is generally supposed, and that is the justification for repeating some of what was contained in the former paper and for adding reports of other cases and for touching on

some recent experimental work that has a direct bearing on this subject.

CLINICAL SYMPTOMS

Most of the patients are middle-aged or elderly men. The heart and blood vessels in many show the evidence of arterial and cardiac sclerosis; the blood pressure may be high. In others no sign of such change is to be made out. In fact, in two of my three cases with necropsy, the only significant vascular sclerosis was in the coronary arteries, the hearts were of normal size, and there had been no hypertension during

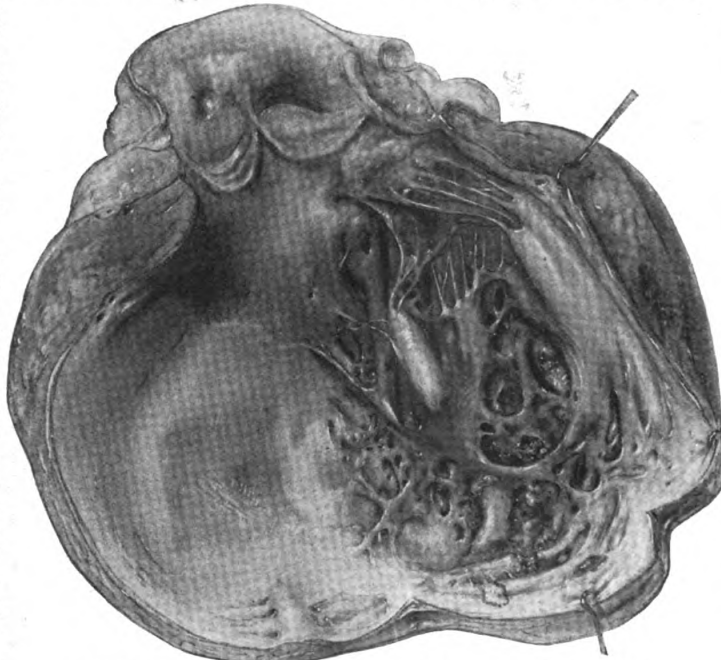


Fig. 1 (Case 3).—Changes on the endocardial surface of left ventricle.

life. In one there was slight involvement of the beginning of the aorta. Previous attacks of angina pectoris may have been experienced. If this has been the case, the patient will describe the attack due to the coronary thrombosis as of unusual severity. Often there is no assignable cause for the attack such as is commonly noted in the typical paroxysmal angina—walking, a heavy meal, undue excitement, etc.—though in some cases these exciting factors seem to provoke the attack or, at least, greatly to aggravate it when it has started. The painful seizure is usually more enduring than in ordinary angina, the spell lasting many minutes or several hours, or a status anginosus developing. The location of the pain, as in the classical angina, is com-

mouse, killed the animal in four or five hours. For a few minutes the animal would not object to the odor of the dye, then it would grow restless and seek to escape, then dyspneic and drowsy and finally unconscious. Before this stage it would recover, if put in the fresh air; after this it would always die. It would become distinctly cyanotic. At necropsy the blood would be almost black and show the presence of methemoglobin by the spectroscope. It now seemed important to try the dye on a human being. This I did on myself, dying my own shoes with some of Toney's preparation. After wearing the shoes four hours, I felt nausea, headache and visual disturbances. Well satisfied with the result of the experiment and enthusiastic for carrying it further on some one else, I removed the shoes. I did not become cyanotic.

November 12, two men in the laboratory, Private Chester Garden and Lieut. E. F. Blair, S. C., having had the matter fully explained to them, volunteered to let me dye their shoes with Toney's dye, by Toney's method. Private Garden was not visibly affected by wearing his shoes six hours, but he complained of headache and nausea, which lasted eighteen hours. Lieutenant Blair, whose shoes were more thoroughly saturated with the dye, after being more thoroughly cleaned with alcohol, became slightly cyanotic in six hours. In seven hours his lips and finger-nails were purple, and he looked ghastly. He had no complaint. His feet "burned" a little, but caused no real discomfort. His blood, obtained by the puncture of the ear lobe, was abnormally dark. The red cells had fallen slightly during the seven hours, from 4,100,000 to 3,900,000. The white cells rose from 9,000 to 12,000, the differential count being unchanged. The hemoglobin by Tallqvist's scale was above 100 and could not be read; it had been 90. By Sahli's it was 95 per cent; it had been 90 per cent. Spectroscopic examination of the blood revealed the normal absorption bands of oxyhemoglobin; sufficient methemoglobin was not present to be detected by a direct vision spectroscope.

NITROBENZENE POISONING

Chemical examination of the dye, later confirmed by the department laboratory, showed the presence of nitrobenzene, also called nitrobenzol, and in trade, oil of mirbane. It is an oily liquid with the odor of bitter almonds, which sometimes produces poisoning in the coal-tar color industries, explosive works, and pharmaceutical laboratories, poisoning whose symptoms are nausea and vomiting, headache, vertigo, tinnitus, visual disturbances, local burning sensation, dyspnea, and marked cyanosis with the formation of methemoglobin. The presence of nitrobenzene in a shoe dye was not surprising to one of the oldest and largest manufacturers of shoe dyes and polishes in this country, since such dyes contain anilin made from nitrobenzene. This firm had never heard of poisoning as a result of wearing dyed shoes.

It is interesting to note that poisoning by nitrobenzene, while unusual, is not unknown. Blyth¹ notes a case in which death of a man resulted in nine hours by the accidental spilling of nitrobenzene on his clothes. It will be surprising if similar cases of cyanosis have not occurred at other camps. I have a record of one case at this camp in which the dye was not bought at Toney's, but at a well known shoe firm

in Jacksonville, which has branch stores in all of the large cities.

The poisonous properties of these dyes are soon lost from the shoes. In three or four days after the shoes have been dyed, it is apparently safe to wear them.

FURTHER OBSERVATIONS ON SEX GLAND IMPLANTATION

G. FRANK LYDSTON, M.D.

CHICAGO

I desire first briefly to present observations of several cases hitherto reported, with special reference to the present condition. The first of these cases was exhibited at the Urological Society of Chicago in October, 1917, and the second at the November, 1917, meeting.

CASES ALREADY REPORTED

CASE 1.—At the age of 17 an injury to the right testis was sustained. This was followed probably by a hematocele and traumatic orchitis. When the swelling subsided the gland had "entirely disappeared." The left testis atrophied to a moderate degree subsequent to the injury. Virility was unimpaired, but the patient developed distinctly feminine secondary sex characteristics.

At the age of 29 an infection of unknown character attacked the remaining testis, with resultant pain in the left ilio-lumbar region, left spermatic cord and testis. The clinical history of the case at that time is not available. According to the patient's story, the testicle did not swell, but there was considerable fullness of the spermatic veins. Within three weeks the organ had completely atrophied, and some weeks later the case was referred to me.

At the time of my examination the patient was of healthy appearance, but excessively fat. The beard was almost negligible, the mammae moderately large, and the pelvis distinctly feminine. Sexual power, which had been "satisfactory" until after the loss of the second testicle, had entirely disappeared. During the years subsequent to the original injury the patient had not been physically as fit as before, and for about a year he had been physically and mentally quite inefficient, which inefficiency rapidly increased after the loss of the remaining testicle.

Palpation disclosed scarcely a vestige of tissue at the end of the spermatic cords. Only a small body somewhat larger than a grain of wheat could be felt on each side. The penis was of very moderate development with a long prepuce, but otherwise normal.

Aug. 1, 1915, I implanted on this patient both testes taken from a boy of 14, dead of a crushing injury. The glands were removed six hours after death and placed in sterile salt solution. The operation was performed thirty-nine hours after the death of the donor.

The results of the implantation were extremely satisfactory, the patient regaining his physical, sexual and mental efficiency. There was a marked change in the secondary sex characteristics so far as the excessive fat was concerned.

Nov. 15, 1918, more than three years and three months subsequent to the operation, the patient reported as still in satisfactory condition. He had entirely lost his fat excess and was robust and athletic in appearance. The implanted testes were still in evidence, firm and obviously sclerotic, and about the size of a good sized hazelnut. The remnants of the testes present at the time of operation had increased to the size of a large pea. There apparently had been no decrease in the size of the implanted organs after the first eighteen months.

CASE 2.—The patient, aged 19, following vaccination at the age of 13, developed a secondary infection of the testes, resulting in almost complete atrophy of both organs within a few weeks. Coincidentally the penis became distinctly smaller. The case was examined by several surgeons, who

1. Blyth, A. B.: Poisons: Their Effects and Detection, New York, the D. Van Nostrand Company, 1907.

diagnosed retained testicle on the left side, and suggested operation. At the age of 17 the patient came under my observation.

The boy was tall and healthy looking, with distinctly feminine secondary sex characteristics. The pelvis, mons veneris, and mammary glands were suggestive of a girl just entering on puberty. No beard was in evidence. There was a bare suggestion of hair on the pubes. The left testicle was a small, soft, barely perceptible nodule about as large as a small pea, just below the external inguinal ring. The right testicle was soft and about the size and shape of a small Lima bean. The penis was no longer than that of a well-developed child of 5 or 6 years of age, slightly "hooded," and suggested an enlarged clitoris. Psychically the boy was normal despite the absence of any signs of virility.

The case passed from under observation and subsequently an ill-advised operation was performed on the left side for "retained testis," with resultant destruction of what little gland tissue remained.

At the age of 19 the boy again reported. Implantation of testes was consented to and the operation performed, Oct. 27, 1916. The material used was taken from a healthy boy, aged 15, dead twenty-four hours of gas poisoning. The glands were refrigerated for thirty-two hours.

The secondary sex characteristics in this case became more masculine, there was a considerable growth of pubic hair, the penis increased greatly in size, and virility was established.

I last examined this patient late in June, 1918, one year and eight months after implantation. The condition of the testes was essentially the same as in Case 1, and apparently they had not grown smaller since the patient was exhibited at the Urological Society in November, 1917. It is interesting to note that this boy passed the Army examination and is now a Second Lieutenant in the U. S. Army in one of our American camps. In a recent letter he reported a considerable increase in the growth of his beard.

ADDITIONAL CASES

CASE 3.—A parietic dement, aged 46, in whom the syphilitic condition had been very insidious, and some six years had elapsed since the symptoms were noticed, had been unable to attend to any business affairs of any consequence for several years and, for obvious reasons, was not permitted to go about the city streets unattended. He complained rather strenuously of loss of sexual power.

In the hope of retarding the progress of the paresis, a successful double implantation was performed in August, 1917. The glands used were taken from a boy, aged 16, dead of accident twenty-four hours. They were refrigerated for thirty hours. The effect of the implantation was in a general way quite remarkable. The patient became brighter and his physical condition greatly improved. Sexual activity was so increased that he was rather inclined to complain of it. His mental condition was so far improved that he was permitted to go about alone, and was able to attend to a little business. It is proper to state that he had antisyphilitic treatment more or less continuously. The fact remains, however, that the case was at a standstill and there was no marked improvement until the implantation was done.

About fourteen months after implantation, the improvement apparently having continued, the patient suddenly developed violent one-sided convulsions, lapsed into coma, and died. There was no necropsy. A diagnosis of probable cerebral thrombosis was made.

CASE 4.—A man, aged 21, whose sexual organs were congenitally undeveloped, had moderately marked feminine secondary sex characteristics, and his beard was very slightly in evidence. His general physical development was imperfect, the patient being 6 feet 3 inches in height and weighing 130 pounds. There was very moderate sexual activity. Unsatisfactory and unpleasurable experimental coitus had been performed on three or four occasions. The patient complained of general weakness and stated that he had very little physical endurance. There was no sexual psychopathy. There was a fair amount of pubic hair and very moderate penile development. Only on painstaking examination could any suggestion

of testes be felt. Several surgeons who previously had examined the patient had diagnosed "retained testes." The glands were about the size of a navy bean, and so soft as to be barely perceptible.

A successful double implantation was performed, June 15, 1918, the material being procured from a boy of 16, dead eighteen hours of a crushing injury of the skull. The material was kept on ice for thirty-six hours.

The patient was examined, Oct. 1, 1918. There had been a marked increase in size and improvement in consistency of the patient's own testes. The physical condition was vastly improved. His color was excellent and he had gained 20 pounds in flesh. As he expressed it, he never felt so well in his life. He said, however, that while erections were more vigorous, he experienced no sexual desire. The penis appeared to be of firmer consistency and slightly better developed than at the time of operation. He had been over-indulging in physical exercise, which possibly might explain the lack of desire. Nov. 12, 1918, improvement in the general condition was sustained, but there was still a lack of sexual desire.

The patient again reported for examination Jan. 6, 1918. There had been still further development of his own testes. The implanted glands were in excellent condition and had not appreciably shrunk since the last examination. Sexual power and desire apparently were normal.

CASE 5.—A professional writer, aged 29, suffered from profound sexual neurasthenia, and complained of the entire gamut of symptoms characteristic of such cases. A careful examination that I made and previous examinations by numerous competent neurologists had elicited no organic nervous lesion. (Since the implantation I have discovered floating right kidney.) The pivotal point of his symptoms was simply pain with extreme hyperesthesia of the skin and pain referred to the bladder. As everything else had been tried in this case, I suggested an implantation, chiefly for the psychic effect.

A successful implantation of a single testis, taken from the body of a boy of 17, dead of accident, and preserved on ice in saline solution for thirty-eight hours, was performed, Sept. 7, 1918.

There was marked improvement in the patient's general condition, but no change in the nervous symptoms of which he complained at the time of the last examination, about six weeks after implantation. The implanted gland was slowly atrophying. Nephropexy was suggested as a "possible" source of improvement. How frequently this operation is disappointing in neuropathies the surgeon is well aware.

CASE 6.—A physician, aged 40, complained of neurasthenic symptoms from overwork, associated with an annoying tachycardia.

Implantation was performed at the patient's request, the companion testicle to the one used in Case 5 being employed. Local results were satisfactory.

The patient has not reported recently, but a month after operation he wrote that he was in much better general condition, and that the tachycardia had subsided.

CASE 7.—A man, past 50 years of age, complained of failure of sexual power. He said that sexual intercourse was possible only when he was under the influence of alcohol. The subject is distinctly melancholic. An implantation was suggested in the hope that the combined psychic effect and the stimulating action of the sex hormone would remedy the obviously psychopathic condition.

Testes taken from a boy of 18, dead of accident, were used, the implantation being done forty-eight hours after the death of the donor. The material was refrigerated for more than thirty hours.

When this case was last heard from, about six weeks after operation, the implanted glands were in excellent condition. The patient stated, however, that he still was unable to perform the act of intercourse except when under the influence of liquor. On one occasion, however, subsequent to the operation, while under the influence of alcohol he indulged, according to his own account, four times in succession, an extent that should be considered excessive for a normal man of his age.

As this patient drifted away from observation, I do not know the present condition of the implanted glands. The patient recently wrote that his sexual status was not improved.

CASE 8.—A man, aged 27, had marked feminine secondary sex characteristics and congenitally undeveloped sexual organs. Not only were the testes almost imperceptible, the case having been pronounced one of retained testes, but there was no scrotal development. In order to prepare a field for implantation, it was necessary to "cup" the scrotal region with a vacuum pump for some weeks prior to the implantation. The pubic hair was exceedingly sparse. There was practically no hair in the normal location of the scrotum. The patient was exceedingly spare, being 5 feet 8¾ inches in height, and weighing 120 pounds. The development of the mons veneris and pelvis was especially feminine in character.

Oct. 8, 1918, a double implantation was performed. The material was taken from a boy of 17, dead of accident. The testes were refrigerated in boric solution on ice for forty-eight hours. The implanted glands in this case were quite large, and the pseudoscrotum which I had succeeded in "pocketing" was so thin that I was very apprehensive of sloughing.

There was sloughing of a circular area of the skin about one-fourth inch in diameter over the most prominent portion of the gland implanted on the right side. There was a slight necrosis of the fascia at this point, and there is still a small sinus giving exit to a small quantity of serous fluid. Five weeks after operation the implanted glands were still in good condition and obviously "alive." There has been an increase in the quantity and an increased coarseness of fiber of the returning pubic hair. Quite a quantity of hair is appearing on the lower part of the scrotum. The patient states that he now has vigorous and prolonged erections and that at the time of erection the penis is distinctly larger than before operation. The organ is slightly firmer when flaccid. The patient's color and general condition is much better, his nutrition having greatly improved.

As to the ultimate results in this case, it is to be remarked that at the age of 27 the outcome is much less promising than in cases in which operation was performed at an earlier period. It is my belief that when implantation is done in cases of like character at an age not too far from puberty, results as good as those obtained in Case 2 reasonably may be expected. In such cases as Case 2 reimplantation should be followed by even more satisfactory results.

Dec. 15, 1918, the sinus had closed and the implanted testes were in good condition.

The next case is especially gratifying to me because the operation was performed by another surgeon. Dr. L. L. Stanley, of the California State Prison at San Quentin, was so courteous as to describe the case to me with permission to publish a report of it in connection with this series.

CASE 9.—A man, aged 25, evidently a moron, committed for attempt at burglary, had been kicked in the testicle, five years previously, with following inflammation, swelling, and subsequent atrophy. At the time of operation the testes were the size of "olive pits." The patient was tall, thin, anemic, and very dull and apathetic. He originally had been a teamster.

The donor was a negro who was hanged for murder. The glands were refrigerated for some hours. The glands were removed from the donor fifteen minutes after death. An anastomosis of the vas deferens was done on the right side. The left "implant" was inserted partially within the tunica vaginalis and held in place by several sutures, without anastomosis. The testes were not decorticated.

Seven weeks after operation the doctor reported that the testes were firm and were not atrophied and were "resting nicely in the scrotal sac." The patient had gained 15 pounds and had become active and alert—in fact, he was improved in every way—and sexually had become very active.

Three months after operation, the right testicle had atrophied slightly, but was still firm and well shaped. The

left testicle was in excellent condition. The doctor said: "He now has erections nightly and frequently in the daytime, something he has never had before. He is much stronger and livelier and gets about much more actively. It is reported that whereas before he was slow and inactive and seemed about 'half dead,' he now speaks out quickly, has improved mentally, and has livened up to a marked degree. He now will 'square away' if anybody 'quips' him, and he can make a quick retort, whereas before he would pay little attention to any offense offered him."

COMMENT

The course of all these cases was practically afebrile and attended by no pain during the postoperative treatment. In Cases 4 and 5 the patients complained of some reflex pains in the spermatic cords for a few weeks subsequent to implantation.

I wish to note especially the result obtained by Dr. Stanley, particularly in the matter of "cross-racial" implantation. Should the testes in this case permanently endure or atrophy no more slowly than when the donor is of the same race as the recipient, it biologically would be a most interesting and a practically valuable observation.

That there is any advantage in the anastomosis of the vas is open to question, first, as to the betterment of nutrition, and secondly, as to the preservation of spermatogenic function. I myself believe that we run more risk of failure of the implant from the greater traumatization of the tissues necessary for anastomosis. Then, too, it is my belief that the spermatogenic epithelium of the tubules degenerates in all cases rather promptly. This, however, is a point that can be determined only by examination of the semen, as to which Dr. Stanley has not yet reported. As bearing on this point, I wish to recall a case of my own in which a fistula formed and persisted for five or six weeks after the implantation of a decorticated gland. The secretion from this fistula contained immature spermatozoa. In dissections that I have made of implanted testes at various times after operation there apparently has been an extensive proliferation of the cells of Leydig and a coincidental encroachment on and destruction of the spermatogenic tissue proper.

An observation which seemingly is worthy of note is the fact that the implanted glands atrophy and disappear more rapidly when the recipient has well-developed testes of his own. The apparently permanent local results thus far obtained were in cases in which the patient had very little gland tissue, as in Cases 1 and 2. A sort of "parasitic" action of the patient's own glands on the implanted organs suggests itself. Possibly the patient's testes appropriate nutritive pabulum which otherwise might be available for the implanted organs. In any event, therapeutic results are obtained and sustained even when the implanted glands eventually disappear. When, as in Cases 1 and 2, the patient's own remnants of testis tissue develop after the implantation, it is reasonable to expect permanence of any improvement that occurs in the patient's condition.

Since this paper was written, I have examined a patient whose case was previously reported, on whom an implantation was done at the age of 69 for possible improvement of senility and failing sexual power. The results in this case were eminently satisfactory, and nearly two years later still endure, although the implanted glands practically have disappeared.

25 East Washington Street.